AMENDMENTS TO THE CLAIMS

1. (previously presented) A purified or isolated polypeptide that comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence set forth in SEQ ID NO: 4;

(b) a fragment of (a) that exhibits aspartyl protease activity involved in processing APP into amyloid beta and includes aspartyl protease active site tripeptides DTG and DSG;

(c) a conservative substitution variant of (a) or (b) having an amino acid sequence identical to (a) or (b) except for conservative substitutions,

wherein the conservative substitution variant comprises an amino acid sequence encoded by a nucleic acid molecule that hybridizes under the following stringent hybridization conditions to the complement of SEQ ID NO: 3:

(1) hybridization at 42°C in a hybridization buffer comprising 6x SSC and 0.1% SDS, and

(2) washing at 65°C in a wash solution comprising 1x SSC and 0.1% SDS;

wherein the conservative substitution variant exhibits aspartyl protease activity involved in processing APP into amyloid beta.

2. (canceled)

3. (currently amended) A purified or isolated polypeptide according to claim 1 ~~or 2,~~ further comprising a heterologous peptide tag.

4. (currently amended) A purified or isolated polypeptide according to claim 1 ~~or~~ 2, wherein the polypeptide lacks a transmembrane domain.

5. (canceled)

6. (currently amended) A method for identifying an agent that decreases the protease activity of an aspartyl protease polypeptide comprising steps of:

(a) expressing the apartyl protease polypeptide of claim 1 ~~or 2~~ by growing a host cell transformed or tranfected with a polynucleotide that encodes the polypeptide, under conditions wherein the cell expressed the polypeptide encoded by the polynucleotide,

(b) measuring proteolytic activity of the polypeptide in the presence and absence of a test agent; and

(c) comparing proteolytic activity of the polypeptide in the presence and absence of the test agent, wherein decreased proteolytic activity in the presence of the test agent identifies the test agent as an agent that decreases the protease activity of the aspartyl protease polypeptide.

7. (previously presented) A method for identifying an agent that decreases the protease activity of an aspartyl protease polypeptide comprising steps of:

(a) expressing an aspartyl protease polypeptide by growing a host cell transformed or transfected with a polynucleotide in the presence and absence of a test agent; under conditions wherein the cell expresses the polypeptide encoded by the polynucleotide,

wherein the polynucleotide comprises a nucleotide sequence that hybridizes under the following stringent hybridization conditions to the complement of SEQ ID NO: 3 or SEQ ID NO: 5:

(1) hybridization at 42°C in a hybridization buffer comprising 6x SSC and 0.1% SDS, and

(2) washing at 65°C in a wash solution comprising 1x SSC and 0.1% SDS;

wherein the polynucleotide encodes a polypeptide comprising a contiguous amino acid sequence that the aspartyl protease active site tripeptides DTG and DSG and exhibits aspartyl protease activity involved in processing APP into amyloid beta,

wherein said polypeptide lacks a transmembrane domain, and

wherein said polypeptide exhibits aspartyl protease activity involved in processing APP into amyloid beta

(b) measuring proteolytic activity of said polypeptide in the presence and absence of a test agent; and

(c) comparing proteolytic activity of the polypeptide in the presence and absence of the test agent, wherein decreased proteolytic activity in the presence of the test agent identifies the test agent as an agent that decreases the protease activity of the aspartyl protease polypeptide.

8. (previously presented) A method according to claim 6 or 7 wherein the proteolytic activity of steps (b) and (c) is proteolytic activity towards an APP substrate.

9. (previously presented) A method according to claim 8, wherein the APP substrate comprises an amyloid beta (A-beta) processing site.

10. (previously presented) A method according to claim 9, wherein the APP substrate comprises the Swedish mutation (K→N, M→L).

11. (previously presented) A method according to claim 9, wherein the APP substrate is a peptide comprising a β-secretase cleavage site that comprises the formula P2-P1-P1'-P2' (SEQ ID NO:74), wherein

P2 is an amino acid selected from K and N;

P1 is an amino acid selected from M and L;

P1' is the amino acid D; and

P2' is the amino acid A.

Claims 12-15 (canceled)

16. (previously presented) An isolated biologically active human aspartyl protease containing a valine at a position which corresponds to position 130 of SEQ ID NO:4, which human aspartyl protease is encoded by a nucleic acid which hybridizes under stringent wash conditions to a nucleic acid encoding the amino acid sequence set forth in SEQ ID NO: 4.

17. (previously presented)An isolated biologically active human aspartyl protease containing a valine at a position which corresponds to position 130 of SEQ ID NO: 4, which human aspartyl protease is encoded by a nucleic acid which is identical across its length to the sequence set forth in SEQ ID NO: 3.

18. (previously presented)An isolated biologically active human aspartyl protease containing a valine at a position which corresponds to position 130 of SEQ ID NO: 4, which human aspartyl protease is encoded by a nucleic acid which is identical to a sequence set forth within SEQ ID NO: 3.

19. (previously presented) An isolated polypeptide with aspartyl protease activity comprising an amino acid sequence which is identical across its length to a sequence in SEQ ID NO: 4.

20. (canceled)